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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,554	10/15/2003	Shafaat A. Rabbani	9471-019-999	7704

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
06/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,554	RABBANI ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-29* is/are pending in the application.

4a) Of the above claim(s) *27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-26 and 28-29* is/are rejected.

7)☐ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/9/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *exhibit A*.

DETAILED ACTION

Election of Species

Applicant's election without traverse of species, antibiotic, in the reply filed on 3/27/2007 is acknowledged. Claims 1-17 are cancelled. Claims 18-29 are pending. After review and reconsideration of the restriction requirement set forth on 9/19/2006, the requirement for the species election is withdrawn. It is noted that claim 27 is withdrawn from consideration as a multiple dependent claim (see objection below). Thus, claims 18-26 and 28-29 are examined on the merits.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 4/9/2007 is/are considered by the examiner and initialed copy/copies of the PTO-1449 is/are enclosed.

Sequence Requirements

In order to have compact prosecution a first office action can be performed on this application, however, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. The disclosure contains sequences that need SEQ ID numbers for figures 1 and 2 or description of drawnings. If these sequences are found in the sequence listing filed 10/15/2003, applicants need only insert the appropriate SEQ ID Nos in figures or figure legends. However, if these sequences are not part of the listing, then applicants need to comply with the sequence rules. Applicant is reminded to check the entire disclosure to ensure that the application is in sequence compliance. Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply (see attached form, PTO *L90)*.

Claim Objections

1. Claim 27 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. Claim 27 depends on claim 25

or 26, which is a multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim 27 has not been further treated on the merits.

2. Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 21 is further drawn to the antibody of claim 18 reciting "the antibody of claim 18, wherein said antibody is ....an anti-idiotypic antibody..", which does not further limit the antibody claim 18 because anti-idiotypic antibody has similar amino acid sequence or structure as the epitope of antigen uPAR, which would be interacted with, but do not have the same binding ability to the same epitope as the anti-human uPAR monoclonal antibody 3936. In order to be a proper dependent claim, the dependent claim should include all the limitation of its base claim. The "anti-idiotypic antibody" in claim 21 does not include all the limitation of the base claim 18, that is, binding to the same epitope recognized by anti-human uPAR antibody 3936.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recites the limitation "wherein said antibody" in line 2 of claim 18. The claim is drawn to an antibody which immunospecifically binds an epitope, wherein said epitope is recognized by anti-human uPAR monoclonal antibody 3936, wherein said antibody is conjugated to ..... It is not clear which of the two antibodies is being referenced by the phrase "said antibody". If the term "said antibody" is referenced to "an antibody", line 1 or claim 18, applicant is suggested to amend claim 18 to "an isolated

antibody which immunospecifically binds an epitope, wherein said epitope ....., wherein said isolated antibody is conjugated.....". Claim 18 renders its dependent claim indefinite.

The lack of clarity could arise where a claim refers to "said lever" or "the lever," where the claim contains no earlier recitation or limitation of a lever and where it would be unclear as to what element the limitation was making reference. Similarly, if two different levers are recited earlier in the claim, the recitation of "said lever" in the same or subsequent claim would be unclear where it is uncertain which of the two levers was intended (See MPEP 2173.05).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 18, 19, and 26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims have been rejected under second paragraph of 35 U.S.C. 112 as insufficient antecedent basis for "said antibody" recited in base claim 18 (see rejection above).

If "said antibody" is referenced to anti-human uPAR monoclonal antibody 3936, (line 2 of claim 18), an antibody (line 1 of claim 18) exists in nature as a naked antibody. The antibody would not constitute patentable subject matter as defined in 35 U.S.C. 101. The claimed invention does not show involvement of the "hand of man". Amending the claims to require that an antibody purified or isolated would indicate the "hand of Man".

If "said antibody" is referenced to an antibody (line 1 of claim 18), and is not the antibody that conjugated to the compound, this antibody does not constitute patentable subject matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 18, 19, 21, 22, and 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Dano et al., (US Patent, 5519120, issued 5/21/1996).

Claim 18 is rejected under 35 U.S.C. 112 2nd (see above) and for this rejection is interpreted as drawn to an antibody, which is immunospecifically binds an epitope being recognized by the anti-human uPAR monoclonal antibody 3936, is conjugated to a cytotoxic compound. Claims 19, 21, and 22 are further drawn to claim 18, wherein the antibody is human antibody, monoclonal antibody or antibody fragment such as Fab fragment. Claims 24 and 25 are further drawn to claim 18, wherein the cytotoxic compound is antibiotic or antimetabolite. Claim 26 is drawn to pharmaceutical composition comprising such.

Dano et al., disclose polyclonal and monoclonal antibodies to urokinase plasminogen activator receptor (uPAR) conjugated (bound) to cancer cytotoxic or cytostatic drug comprising antibiotics such as doxorubicin and antimetabolite such as methotrexate and pharmaceutical composition or medicament comprising such for inhibiting plasminogen activation in cells (col 15-16, col 61-62, and col 72-73,example 7). Dano et al., disclose the antibodies to uPAR are human antibody or antibody binding fragment thereof, such as the Fab fragment (col 21, line 61-col 22, line 1-8). Dano et al., further disclose the

antibody inhibiting the interaction between urokinase plasminogen activator (uPA) and its receptor, uPAR (example 7, col, 73 and figure 24).

The prior art (anti uPAR antibody conjugate) appears to meet the requirements of the instant claims regarding the immunospecifically binding to an epitope recognized by the anti-human uPAR monoclonal antibody 3936 because the antibodies disclosed by Dano et al., have the same function as the monoclonal anti-uPAR antibody 3936 for inhibiting uPA/uPAR interaction as evidenced by Stahl et al., (Cancer Research, vol 54, page 3068, col 1, para 1, 1994). Regarding the same epitope based on the amino acid sequence of uPAR, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material and structural characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

1. Claims 18-22, 24, 26, 28-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Pessara et al., (US Patent, 6025142, filing date, Jun 2, 1995).

Claims 18, 19, 21, 22, 24-26, and 27 are set forth above. Claim 20 is further drawn to claim 18, wherein the antibody is humanized antibody. Claims 28-29 are drawn to humanized antibody, which immunospecifically binds an epitope, wherein said epitope is recognized by the anti-human uPAR monoclonal antibody 3936 and a pharmaceutical composition comprising such.

Pessara et al., disclose monoclonal antibodies to urokinase plasminogen activator receptor (uPAR) conjugated to cancer cytotoxic drug comprising antibiotics such as doxorubicin and therapeutic or pharmaceutical agent comprising the antibody conjugate for treating cancer by inhibiting interaction of urokinase plasminogen activator (uPA) and its receptor, uPAR (col 8-10, specifically col 8, para 9-10; col 9, para 1; col 10 para 3-4). Pessara et al., disclose the antibodies to uPAR are human, humanized antibodies or antibody binding fragments thereof, such as the Fab, $F(ab')_2$, FV, etc. (col 9, para 2-4). Pessara et al., further disclose that conjugate of the antibodies in particular human or humanized

antibodies for in vivo using and administration (col 10, para 3-4). Pessara et al., specifically disclose the antibodies are capable of inhibiting the interaction between u-PA and uPAR (col 3, para 1).

The prior art (anti uPAR antibody conjugate) appears to meet the requirements of the instant claims regarding the immunospecifically binding to an epitope recognized by the anti-human uPAR monoclonal antibody 3936 because the antibodies disclosed by Pessara et al., perform the same function as the monoclonal anti-uPAR antibody 3936 for inhibiting uPA/uPAR interaction as evidenced by Stahl et al., (Cancer Research, vol 54, page 3068, col 1, para 1, 1994). Regarding the same epitope based on the amino acid sequence of uPAR, the Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material and structural characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquires set forth in Graham V. john Deere Co., 383 U.S. 1, 148 USPQ 459 (1996), that are applied for establishing a background for determining obviousness under 25 U.S. C. 103 (a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or obviousness.

Claims 18 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dano et al., (US Patent, 5519120, issued 5/21/1996) in view of Stahl et al., (Cancer Research, vol 54, page 3066-3071, 1994).

The claims 18 and 24-26 are set forth above. Claim 23 is further drawn to monoclonal antibody to human uPAR, 3936.

The teaching of Dano et al., is set forth above.

Dano et al., does not teach monoclonal antibody 3936.

Stahl et al., teach mouse anti-human uPAR mAb 3936 (page 3066, col 2).

One of ordinary skill in the art at the time the invention was made would have been motivated to replace the antibody in the conjugate taught by Dano et al., with the anti-human uPAR mAb 3936 taught by Stahl et al., in order to benefit the cancer treatment by inhibition of cancer cell metastasis induced by the interaction of uPA and its receptor uPAR because Stahl et al., teach that uPAR mAb 3936 specifically recognizes the uPA-binding site of uPAR and receptor binding of uPA is required for the invasion or metastasis of cancer cells, such as melanoma cells (page 3068, col 1) and Dano et al., also teach treating a cancer condition by targeting uPAR on the surface of the cells (col 13, para 2). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for making the anti-uPAR mAB 3936 conjugate or pharmaceutical composition comprising the antibody conjugate by combining the teaching of Dano et al., with the teaching of Stahl et al., because Dano et al., have shown how to obtain an anti-uPAR antibody conjugated to a cytotoxic agent and composition comprising the antibody conjugate for treating a disease condition and Stahl et al., have shown anti-human uPAR mAb 3936.

Deposit of mouse anti-human uPAR mAb 3936

It is noted that the claimed invention relies on a biological material, anti-human uPAR mAb 3936 requiring a biological deposit to satisfy the statutory requirements for patentability under 35 U.S.C. 112. Applicant refers to page 27 of the specification that the antibody obtained from American Diagnostica Inc., Greenwich, CT. The art also discloses that uPAR mAb 3936 is commercially available at American

Diagnostica Inc., Greenwich, CT as evidenced by Stahl et al., (Cancer Research, vol 54, page 3066, col 2, 1994, see rejection above) and by catalog/data sheet of American Diagnostica Inc. (exhibit A), which all indicate availability to the public of the claimed antibody, uPAR mAb 3936. Accordingly, the Office does not further require deposit of uPAR mAb 3936.

The Office will accept commercial availability as evidence that a biological material is known and readily available only when the evidence is clear and convincing that the public has access to the material. See the final rule entitled "Deposit of Biological Materials for Patent Purposes," 54 FR 34864, 34875 (August 22, 1989). A product could be commercially available but only at a price that effectively eliminates accessibility to those desiring to obtain a sample. The relationship between the applicant relying on a biological material and the commercial supplier is one factor that would be considered in determining whether the biological material was known and readily available. However, the mere fact that the biological material is commercially available only through the patent holder or the patent holder's agents or assigns shall not, by itself, justify a finding that the necessary material is not readily available, absent reason to believe that access to the biological material would later be improperly restricted. See MPEP (2401.01).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao,
Examiner
Art Unit 1642

LY

SHANON FOLEY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice to Comply	Application No. 10687554	Applicant(s) Rabbani et al	
	Examiner Lei Yao	Art Unit 1642	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: need SEQ ID numbers for sequences listed in figure 1 and 2.

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
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